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Biological Interaction of Selenium with Other Trace Elements in Chicks

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Studies were conducted to determine whether or not elements whose valence shell of electrons was similar to that of selenium would reverse the toxicity of selenium to chicks. The elements studied were arsenic, tellurium, tin, and lead. Each of these elements, when added to the diet of chicks, reversed the toxicity of 25 ppm selenium as measured by weight gain. In spite of the protection afforded by these elements, there was no decrease in liver concentration of selenium except with levels of arsenic higher than that needed for reversal of toxicity.

The discovery that the biological effects of selenium could be modified by other elements dates back to the work of Moxon (*1*), who reported that arsenic counteracted the toxic effects of seleniferous grain. This was found to be true in rats (*1*), pigs (*2*), dogs (*3*), and chicks (*4*). Sulfate has also been shown to counteract the toxicity of selenium in plants (*5, 6*), bacteria (*7, 8*), as well as animals (*9–11*). More recently a biological interaction of selenium with mercury has been discovered. Ganther et al. (*12*) reported that selenium would counteract the toxicity of methylmercury, and Hill (*13*) reported that mercury would counteract the toxic effects of selenium. In the latter instance, the inclusion of either cadmium or copper also ameliorated the toxic effects of selenium. The reaction products resulting from the mixing of $HgCl_2$, $CdSO_4$, or $CuSO_4$ with SeO_2 were less toxic to chicks than the same amount of selenium fed as SeO_2.

The mechanism underlying these interactions is unknown. The tissue levels of selenium or of the element with which selenium interacts are not necessarily reduced. Ganther and Baumann (*11*) reported that the injection of cadmium tended to increase the retention of selenium in rats. Johnson and Pond (*14*) found that mercuric compounds increased the kidney levels of selenium. A similar finding was reported by Parizek et al. (*15*), who injected pregnant mice with radioactive selenium in the presence and absence of mercury. As the mercury level was increased there was an increased amount of selenium in the blood and liver of the dams, but the fetuses contained less. Parizek et al. (*16*) also reported that the administration of cadmium with selenium resulted in increased blood levels of selenium, while administration of selenium with mercury caused higher blood levels of mercury. Gunn, Gould, and Anderson (*17*) found that selenium would protect mouse testes from vascular injury caused by cadmium but that the testes concentration of cadmium and selenium was higher in those animals receiving both the elements than in those receiving either element alone.

All of the studies referred to above indicate that the biological effects of selenium can be modified by several elements. Hill and Matrone (*18*) proposed that elements whose valence shell electronic structures were similar would act antagonistically to each other biologically because their chemical properties are so similar. In the work cited above, arsenic and sulfur could fulfill this criterion in relation to selenium. There are other elements whose valence shell electronic structures are also similar to that of selenium. These are tellurium, tin, and lead. The purpose of the work presented here was to determine whether or not these elements as well as arsenic would affect the toxic manifestation of selenium in chicks and to determine if they affected the selenium concentration in the liver.

Materials and Methods

Day-old chicks were used in all the experiments. They were housed in conventional, electrically-

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heated, battery brooders with raised wire floors. Feed and water were available *ad libitum*. The composition of the basal diet is presented in Table 1.

Selenium was added to the diet as selenous acid, arsenic as arsenic trichloride, tellurium as potassium tellurite, tin and lead as the dichlorides. Selenium concentration in the livers was determined spectrofluorimetrically by the method of Olson, Palmer, and Cary (*19*). The statistical significance of the differences observed was evaluated by analysis of variance and by the use of Tukey's least significant differences (*20*).

Table 1. Basal diet.

Ingredients	Content, %
Ground yellow corn	52.75
Soybean meal (44% protein)	40.00
Defluorinated rock phosphate	3.20
Cottonseed oil[a]	3.00
NaCl	0.50
$MnSO_4$	0.02
DL-Methionine	0.31
Vitamin mix[b]	0.22

[a] Wesson Oil, Hunt-Wesson Foods, Fullerton, Ca.
[b] Supplies per kg feed: retinyl acetate, 4500 I.U.; cholecalciferol, 600 I.C.U.; menadione sodium bisulfite, 1.6 mg; DL-α-tocopherol acetate, 10 mg; thiamine HCl, 5.4 mg; riboflavin, 10.8 mg; calcium pantothenate, 30 mg; niacin, 81 mg; pyridoxine HCl, 9 mg; folacin, 3.6 mg; biotin, 0.27 mg; vitamin B_{12}, 0.027 mg.

Results and Discussion

In the first experiment, selenium was fed at 25 ppm and arsenic at 10, 30, and 50 ppm in combination with selenium. The results are presented in Table 2. Arsenic at 50 ppm was slightly toxic, as the reduction in weight gain shows. However, as little as 10 ppm arsenic largely overcame the growth retardation and mortality caused by 25 ppm selenium. At this level of arsenic there was no effect on the liver selenium concentration. As the arsenic level was increased in the diet, there was a decrease in selenium concentration in the liver but there was no concomitant significant increase in weight gain to indicate that the selenium toxicity was lessened.

In a similar type of experiment, tellurite was tested for interaction with selenium with the results shown in Table 3. Preliminary studies had indicated that much higher levels of tellurite were necessary for interaction than was necessary for arsenic. Tellurite was itself toxic at 500 ppm, as shown by the weight gain reduction although previous studies had shown that 200 ppm was not a toxic level. There was a significant interaction of tellurite with

Table 2. Effects of arsenic on selenium toxicity.

Element (and level, ppm)	Wt. gain, g[a]	Mortality, %	Liver Se, ppm[b]
Control	306	6.6	0.17
Se(25)	65	46.6	3.43
As(50)	249	16.6	0.14
Se(25) + As(10)	235	3.3	4.10
Se(25) + As(30)	268	13.3	2.55
Se(25) + As(50)	250	36.6	2.24
$W_{.05}$[c]	48.2	31.8	0.865

[a] 21 day gain; means of three lots of 10 chicks each.
[b] Means of 8 chicks per treatment.
[c] Tukey's honestly significant difference $p < 0.05$.

Table 3. Effects of tellurium (K_2TeO_3) on selenium toxicity.

Element (and level, ppm)	Wt. gain g[c]	Mortality, %	Liver Se, ppm[b]
Control	453	6.6	0.20
Se(25)	83	48.0	3.77
Te(500)	174	12.0	0.50
Se(25) + Te(100)	152	18.0	3.94
Se(25) + Te(300)	139	14.0	5.33
Se(25) + Te(500)	135	25.0	5.64
$W_{.05}$[c]	42.8	22.5	1.81

[a] 21 day gain; means of five lots of 10 chicks each.
[b] Means of 8 chicks per treatment.
[c] Tukey's honestly significant difference, $p < 0.05$.

selenium indicating that tellurite could also counteract the toxicity of selenium as measured by weight gain and mortality. In this instance, as with 10 ppm arsenic, there was no reduction in liver selenium concentration as a result of the interaction.

The results of an experiment to test the interaction of tin with selenium are presented in Table 4. Tin was not toxic at the highest level used, 200 ppm. Increasing levels of this element from 50 to 200 ppm reduced the growth-retarding effect of selenium. There was no reduction in liver selenium concentration with increasing levels of tin.

The effects of lead on selenium toxicity are presented in Tables 5 and 6. Lead at 200 ppm was not toxic to the chicks. While the reversal of selenium toxicity by this level of lead was not statistically significant at the 5% level of probability, it approached it. At this level of lead the selenium concentration of the liver increased significantly. The results of feeding 400 ppm lead are presented in Table 6. The effect of the interaction of lead and selenium on the growth of the chicks was statistically significant indicating that lead is effective in counteracting selenium toxicity.

The results of these studies extend the list of ele-

Table 4. Effects of tin on selenium toxicity.

Element (and level, ppm)	Wt. gain, g[a]	Mortality, %	Liver Se, ppm[b]
Control	346	0	0.18
Se(25)	64	6.6	3.30
Sn(200)	352	3.3	0.11
Se(25) + Sn(50)	86	6.6	3.74
Se(25) + Sn(100)	119	16.6	3.93
Se(25) + Sn(200)	134	3.3	3.65
$W_{.05}$[c]	39.3	N.S.	1.11

[a] 21 day gain; means of three lots of 10 chicks each.
[b] Means of 8 chicks per treatment.
[c] Tukey's honestly significant difference, $p < 0.05$.

Table 5. Effects of lead on selenium toxicity.

Element (and level, ppm)	Wt. gain, g[a]	Mortality, %	Liver Se, ppm[b]
Control	374	0	0.18
Se(25)	49	0	3.53
Pb(200)	392	0	0.16
Se(25) + Pb(50)	62	0	4.75
Se(25) + Pb(100)	67	0	4.00
Se(25) + Pb(200)	75	3.3	6.01
$W_{.05}$[c]	32.7	N.S.	1.664

[a] 21 day gain; means of three lots of 10 chicks each.
[b] Means of 8 chicks per treatment.
[c] Tukey's honestly significant difference, $p < 0.05$.

Table 6. Interaction of lead and selenium.

Element (and level, ppm)	Wt. gain, g[a]	Mortality, %
Control	399	2.5
Se(20)	111	5.0
Pb(400)	393	2.5
Se(20) + Pb(400)	211[b]	0

[a] 20 day gain; means of four lots of 10 chicks each.
[b] Significant interaction, $p < 0.01$.

ments which interact biologically with selenium to include tellurium, tin, and lead. Thus all of the elements whose valence shell electronic structure may be similar to that of selenium have been shown to interact with this element in that the growth regarding effects of selenium are reduced.

From the studies conducted thus far, the mechanisms underlying the interactions are not clear. Levander and Baumann (*21*) reported that the presence of arsenic increased the biliary excretion of selenium and the results presented here indicate that the liver concentration is reduced by arsenic at levels of 30 and 50 ppm. However, 10 ppm arsenic was as effective in counteracting selenium toxicity as the higher levels, but no reduction in liver selenium concentration was observed at that level of arsenic. The finding that none of the interactants studied here reduced the concentration of selenium in the liver would seem to preclude absorption and/or retention as the locus of the interaction.

The finding that the counteraction of selenium toxicity by elements with electronic structure similar to that of selenium does not reduce liver selenium concentration is not unique. Jensen (*22*) reported that both copper and silver overcame growth retardation of chicks by selenium but increased the liver selenium.

If the liver is, in fact, a representative organ for selenium accumulation in the presence of biological interactants, then it would seem appropriate to pursue the mechanistic studies by investigating selenium distribution within the organelles of the cell and to determine the form in which selenium is present in the liver. These studies are now underway in our laboratory.

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